

SEQUENCE LISTING

<110> Wadhwa, Ren Sugihara, Takas RADELLE Ohide, Akiko

<120> TUMOR SUPPRESSOR GENE

<130> 06501-091001

<140> US 10/045,815

<141> 2001-10-26

<150> PCT/JP00/02731

<151> 2000-04-26

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<170> FastSEQ for Windows Version 4.0

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Val Arg Ala Leu Lys Leu Thr Thr Leu Leu Ala Val Val Ala Ala
5 10 15

gcc tcc caa gcc gag gtc gag tcc gag gca gga tgg ggc atg gtg acg
Ala Ser Gln Ala Glu Val Glu Ser Glu Ala Gly Trp Gly Met Val Thr
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cct gat ctg ctc ttc gcc gag ggg acc gca gcc tac gcg cgc ggg gac

Pro Asp Leu Leu Phe Ala Glu Gly Thr Ala Ala Tyr Ala Arg Gly Asp

35 40 45 50

tgg ccc ggg gtg gtc ctg agc atg gaa cgg gcg ctg cgc tcc cgg gca 249
Trp Pro Gly Val Val Leu Ser Met Glu Arg Ala Leu Arg Ser Arg Ala
55 60 65

gcc ctc cgc gcc ctt cgc ctg cgc tgc cgc acc cag tgt gcc gcc gac 297
Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr Gln Cys Ala Ala Asp
70 75 80

| ttc Phe | ccg Pro | tgg Trp 85 | Glu | ctg Leu | gac Asp | ccc Pro | gac Asp 90 | Trp | tco Ser | ccc Pro | ago Ser | c ccg Pro | Ala | cag Gln | gcc Ala | 345 |
|-------------------|-------------------|-------------------|-------------------|-------------------|------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| tcg Ser | ggc Gly 100 | Ala | ggc | gcc Ala | ctg Leu | cgc Arg 105 | gac Asp | ctg Leu | ago Ser | ttc Phe | ttc Phe | Gly | ggc | ctt Leu | ctg Leu | 393 |
| cgt Arg 115 | Arg | gct Ala | gcc Ala | tgc Cys | ctg Leu 120 | cgc Arg | cgc Arg | tgc Cys | cto Leu | ggg Gly 125 | Pro | ccg Pro | gcc Ala | gcc Ala | cac His 130 | 441 |
| tcg Ser | ctc Leu | agc Ser | gaa Glu | gag Glu 135 | atg Met | gag Glu | ctg Leu | gag Glu | ttc Phe 140 | Arg | aag Lys | cgg Arg | agc Ser | ccc Pro 145 | Tyr | 489 |
| aac Asn | tac Tyr | ctg Leu | cag Gln 150 | gtc Val | gcc Ala | tac Tyr | ttc Phe | aag Lys 155 | atc Ile | aac Asn | aag Lys | ttg Leu | gag Glu 160 | aaa Lys | gct Ala | 537 |
| gtt Val | gct Ala | gca Ala 165 | gca Ala | cac His | acc Thr | ttc Phe | ttc Phe 170 | gtg Val | ggc | aat Asn | cct Pro | gag Glu 175 | cac His | atg Met | gaa Glu | 585 |
| atg Met | cag Gln 180 | cag Gln | aac Asn | cta Leu | gac Asp | tat Tyr 185 | tac Tyr | caa Gln | acc Thr | atg Met | tct Ser 190 | gga Gly | gtg Val | aag Lys | gag Glu | 633 |
| gcc Ala 195 | gac Asp | ttc Phe | aag Lys | gat Asp | ctt Leu 200 | gag Glu | act Thr | caa Gln | ccc Pro | cat His 205 | atg Met | caa Gln | gaa Glu | ttt Phe | cga Arg 210 | 681 |
| ctg Leu | gga Gly | gtg Val | cga Arg | ctc Leu 215 | tac Tyr | tca Ser | gag Glu | gaa Glu | cag Gln 220 | cca Pro | cag Gln | gaa Glu | gct Ala | gtg Val 225 | ccc Pro | 729 |
| cac His | cta Leu | gag Glu | gcg Ala 230 | gcg Ala | ctg Leu | caa Gln | gaa Glu | tac Tyr 235 | ttt Phe | gtg Val | gcc Ala | tat Tyr | gag Glu 240 | gag Glu | tgc Cys | 777 |
| cgt Arg | gcc Ala | ctc Leu 245 | tgc Cys | gaa Glu | gl ^y aaa | ccc Pro | tat Tyr 250 | gac Asp | tac Tyr | gat Asp | ggc Gly | tac Tyr 255 | aac Asn | tac Tyr | ctt Leu | 825 |
| gag Glu | tac Tyr 260 | aac Asn | gct Ala | gac Asp | Leu | ttc Phe 265 | cag Gln | gcc Ala | atc Ile | aca Thr | gat Asp 270 | cat His | tac Tyr | atc Ile | cag Gln | 873 |
| gtc Val 275 | ctc Leu | aac Asn | tgt Cys | Lys | cag Gln 280 | aac Asn | tgt Cys | gtc Val | acg Thr | gag Glu 285 | ctt Leu | gct Ala | tcc Ser | cac His | cca Pro 290 | 921 |
| agt Ser | cga Arg | gag Glu | Lys | ccc Pro 295 | ttt Phe | gaa g Glu . | gac Asp | ttc Phe | ctc Leu 300 | cca Pro | tcg Ser | cat His | Tyr | aat Asn 305 | tat Tyr | 969 |

| ctg cag ttt gcc tac tat aac att ggg aat tat aca caa gct ggt gaa Leu Gln Phe Ala Tyr Tyr Asn Ile Gly Asn Tyr Thr Gln Ala Gly Glu 310 315 320 | 1017 |
|--|--|
| tgt gcc aag acc tat ctt ctc ttc ttc ccc aat gac gag gtg atg aac Cys Ala Lys Thr Tyr Leu Leu Phe Phe Pro Asn Asp Glu Val Met Asn 325 330 335 | 1065 |
| caa aat ttg gcc tat tat gca gct atg ctt gga gaa gaa cac acc aga Gln Asn Leu Ala Tyr Tyr Ala Ala Met Leu Gly Glu Glu His Thr Arg 340 345 350 | 1113 |
| tcc atc ggc ccc cgt gag cag ggc acc tagggaaaga tgtgaccccg Ser Ile Gly Pro Arg Glu Gln Gly Thr 355 360 | 1160 |
| gaaagtactc agtttecctg ccctggagtg ccaaggagta ccgacagcga agcctactgg aaaaagaact gcttttcttc gcttatgatg ttttttggaat tccctttgtg gatcgggatt catggactcc agaagaaatg atteccaaga aattgcaaga gaaacagaag tgaggacctt gaagaacatg catggttgga tcagtctgat gaagcacttg agggttggcct ggaatgcagt cctcagaagcg gttggtcca taggtcggcc ggaatgcagt cctcagaagcg gttggtca taggtcagaa ccgtacgcat ctcccagaga attgggaacc ttatgaagga aattgggaac cttgggaaggagg cccctctgagaaga gagacacag gagtactg aggatggacag gactgacccg ggaaggtgc cccctgctgt atgaaggcat cagtctcacc atgaactcca actacctcaga tagtcacag aggatgcac cagggtaga cacctcagg aggatgcac cagggtaga cacctcaga aggatgcac cagggtaga cacctcaga aggatgcac cagggtaga cacctcaga aggatgcac cggggtagaa cctccccaac atggggaaact gacctcagag ggggccaacc ggacggtaga cacctcagag gagacgaac caggggagaaga aagggcaac aatggggaag ggggccaacct gacctacaac gtgacggaaa aagggcaaagt gactactcag gcctggatac gccctctac ttttcctact ctcatctggt gtgcgcaact gccatcctac atgccgaga aggagaagg gatgatagtc atccagtcac ggtggacaact gccatcctta cctaaatggg gacttcgatg gcggaaactt ttatttcact gccagaacctggaagaaggaaggaaggaaggaaggaagaaggaag | 1220 1280 1340 1400 1460 1520 1580 1700 1760 1820 1880 1940 2060 2120 2300 2420 2480 2540 2660 2720 2780 2829 |
| Val Thr Pro Asp Leu Leu Phe Ala Glu Gly Thr Ala Ala Tyr Ala Arg 35 40 45 | |

4

Gly Asp Trp Pro Gly Val Val Leu Ser Met Glu Arg Ala Leu Arg Ser Arq Ala Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr Gln Cys Ala 75 70 Ala Asp Phe Pro Trp Glu Leu Asp Pro Asp Trp Ser Pro Ser Pro Ala 90 Gln Ala Ser Gly Ala Gly Ala Leu Arg Asp Leu Ser Phe Phe Gly Gly 105 Leu Leu Arg Arg Ala Ala Cys Leu Arg Arg Cys Leu Gly Pro Pro Ala 120 Ala His Ser Leu Ser Glu Glu Met Glu Leu Glu Phe Arg Lys Arg Ser 135 Pro Tyr Asn Tyr Leu Gln Val Ala Tyr Phe Lys Ile Asn Lys Leu Glu 150 155 Lys Ala Val Ala Ala Ala His Thr Phe Phe Val Gly Asn Pro Glu His 170 Met Glu Met Gln Gln Asn Leu Asp Tyr Tyr Gln Thr Met Ser Gly Val 180 185 190 Lys Glu Ala Asp Phe Lys Asp Leu Glu Thr Gln Pro His Met Gln Glu 200 Phe Arg Leu Gly Val Arg Leu Tyr Ser Glu Glu Gln Pro Gln Glu Ala 220 215 Val Pro His Leu Glu Ala Ala Leu Gln Glu Tyr Phe Val Ala Tyr Glu 230 235 Glu Cys Arg Ala Leu Cys Glu Gly Pro Tyr Asp Tyr Asp Gly Tyr Asn 255 245 250 Tyr Leu Glu Tyr Asn Ala Asp Leu Phe Gln Ala Ile Thr Asp His Tyr 265 Ile Gln Val Leu Asn Cys Lys Gln Asn Cys Val Thr Glu Leu Ala Ser 280 His Pro Ser Arg Glu Lys Pro Phe Glu Asp Phe Leu Pro Ser His Tyr 295 300 Asn Tyr Leu Gln Phe Ala Tyr Tyr Asn Ile Gly Asn Tyr Thr Gln Ala 310 315 Gly Glu Cys Ala Lys Thr Tyr Leu Leu Phe Phe Pro Asn Asp Glu Val 325 330 Met Asn Gln Asn Leu Ala Tyr Tyr Ala Ala Met Leu Gly Glu Glu His 345 Thr Arg Ser Ile Gly Pro Arg Glu Gln Gly Thr 360 <210> 3 <211> 2600 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (52)...(2259) <400>3ctccggcctt ggtggcggt ggctggcggt tccgttaggt ctgagggagc g atg gcg 57 Met Ala

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Val Arg Ala Leu Lys Leu Leu Thr Thr Leu Leu Ala Val Val Ala Ala

105

10 gcc tcc caa gcc gag gtc gag tcc gag gca gga tgg ggc atg gtg acg 153 Ala Ser Gln Ala Glu Val Glu Ser Glu Ala Gly Trp Gly Met Val Thr cet gat etg etc tte gee gag ggg ace gea gee tae geg ege ggg gae 201 Pro Asp Leu Leu Phe Ala Glu Gly Thr Ala Ala Tyr Ala Arg Gly Asp 45 tgg ccc ggg gtg gtc ctg agc atg gaa cgg gcg ctg cgc tcc cgg gca 249 Trp Pro Gly Val Val Leu Ser Met Glu Arg Ala Leu Arg Ser Arg Ala 60 55 gee etc ege gee ett ege etg ege tge ege acc eag tgt gee gee gae 297 Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr Gln Cys Ala Ala Asp 70 ttc ccg tgg gag ctg gac ccc gac tgg tcc ccc agc ccg gcc cag gcc 345 Phe Pro Trp Glu Leu Asp Pro Asp Trp Ser Pro Ser Pro Ala Gln Ala 85 teg gge gee gge gee etg ege gae etg age tte tte ggg gge ett etg 393 Ser Gly Ala Gly Ala Leu Arg Asp Leu Ser Phe Phe Gly Gly Leu Leu 100 441 Arg Arg Ala Ala Cys Leu Arg Arg Cys Leu Gly Pro Pro Ala Ala His tcg ctc agc gaa gag atg gag ctg gag ttc cgc aag cgg agc ccc tac 489 Ser Leu Ser Glu Glu Met Glu Leu Glu Phe Arg Lys Arg Ser Pro Tyr 135 aac tac ctg cag gtc gcc tac ttc aag atc aac aag ttg gag aaa gct 537 Asn Tyr Leu Gln Val Ala Tyr Phe Lys Ile Asn Lys Leu Glu Lys Ala 150 gtt gct gca gca cac acc ttc ttc gtg ggc aat cct gag cac atg gaa 585 Val Ala Ala His Thr Phe Phe Val Gly Asn Pro Glu His Met Glu 175 165 atg cag cag aac cta gac tat tac caa acc atg tet gga gtg aag gag 633 Met Gln Gln Asn Leu Asp Tyr Tyr Gln Thr Met Ser Gly Val Lys Glu 180 gcc gac ttc aag gat ctt gag act caa ccc cat atg caa gaa ttt cga 681 Ala Asp Phe Lys Asp Leu Glu Thr Gln Pro His Met Gln Glu Phe Arg 210 200 195 ctg gga gtg cga ctc tac tca gag gaa cag cca cag gaa gct gtg ccc 729 Leu Gly Val Arg Leu Tyr Ser Glu Glu Gln Pro Gln Glu Ala Val Pro 225 215 777 cac cta gag gcg gcg ctg caa gaa tac ttt gtg gcc tat gag gag tgc His Leu Glu Ala Ala Leu Gln Glu Tyr Phe Val Ala Tyr Glu Glu Cys 235 230

| cgt Arg | gcc Ala | ctc Leu 245 | tgc Cys | gaa Glu | gly | ccc Pro | tat Tyr 250 | gac Asp | tac Tyr | gat Asp | ggc Gly | tac Tyr 255 | aac Asn | tac Tyr | ctt Leu | 825 |
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| gag Glu | tac Tyr 260 | aac Asn | gct Ala | gac Asp | ctc Leu | ttc Phe 265 | cag Gln | gcc Ala | atc Ile | aca Thr | gat Asp 270 | cat His | tac Tyr | atc Ile | cag Gln | 873 |
| gtc Val 275 | ctc Leu | aac Asn | tgt Cys | aag Lys | cag Gln 280 | aac Asn | tgt Cys | gtc Val | acg Thr | gag Glu 285 | ctt Leu | gct Ala | tcc Ser | cac His | cca Pro 290 | 921 |
| agt Ser | cga Arg | gag Glu | aag Lys | ccc Pro 295 | ttt Phe | gaa Glu | gac Asp | ttc Phe | ctc Leu 300 | cca Pro | tcg Ser | cat His | tat Tyr | aat Asn 305 | tat Tyr | 969 |
| ctg Leu | cag Gln | ttt Phe | gcc Ala 310 | tac Tyr | tat Tyr | aac Asn | att Ile | ggg Gly 315 | aat Asn | tat Tyr | aca Thr | caa Gln | gct Ala 320 | ggt Gly | gaa Glu | 1017 |
| tgt Cys | gcc Ala | aag Lys 325 | acc Thr | tat Tyr | ctt Leu | ctc Leu | ttc Phe 330 | ttc Phe | ccc Pro | aat Asn | gac Asp | gag Glu 335 | gtg Val | atg Met | aac Asn | 1065 |
| caa Gln | aat Asn 340 | ttg Leu | gcc Ala | tat Tyr | tat Tyr | gca Ala 345 | gct Ala | atg Met | ctt Leu | gga Gly | gaa Glu 350 | gaa Glu | cac His | acc Thr | aga Arg | 1113 |
| tcc Ser 355 | atc Ile | ggc Gly | ccc Pro | cgt Arg | gag Glu 360 | agt Ser | gcc Ala | aag Lys | gag Glu | tac Tyr 365 | cga Arg | cag Gln | cga Arg | agc Ser | cta Leu 370 | 1161 |
| ctg Leu | gaa Glu | aaa Lys | gaa Glu | ctg Leu 375 | ctt Leu | ttc Phe | ttc Phe | gct Ala | tat Tyr 380 | gat Asp | gtt Val | ttt Phe | gga Gly | att Ile 385 | ccc Pro | 1209 |
| ttt Phe | gtg Val | gat Asp | ccg Pro 390 | gat Asp | tca Ser | tgg Trp | act Thr | cca Pro 395 | gaa Glu | gaa Glu | gtg Val | att Ile | ccc Pro 400 | aag Lys | aga Arg | 1257 |
| ttg Leu | caa Gln | gag Glu 405 | aaa Lys | cag Gln | aag Lys | tca Ser | gaa Glu 410 | cgg Arg | gaa Glu | aca Thr | gcc Ala | gta Val 415 | cgc Arg | atc Ile | tcc Ser | 1305 |
| cag Gln | gag Glu 420 | att Ile | gly aaa | aac Asn | ctt Leu | atg Met 425 | aag Lys | gaa Glu | atc Ile | gag Glu | acc Thr 430 | ctt Leu | gtg Val | gaa Glu | gag Glu | 1353 |
| aag Lys 435 | acc Thr | aag Lys | gag Glu | tca Ser | ctg Leu 440 | gat Asp | gtg Val | agc Ser | aga Arg | ctg Leu 445 | acc Thr | cgg Arg | gaa Glu | ggt Gly | ggc Gly 450 | 1401 |
| ccc Pro | ctg Leu | ctg Leu | tat Tyr | gaa Glu 455 | ggc Gly | atc Ile | agt Ser | ctc Leu | acc Thr 460 | atg Met | aac Asn | tcc Ser | aaa Lys | ctc Leu 465 | ctg Leu | 1449 |

| | ggt Gly | | | | | | | | | | | | | | | 1497 |
|-----|-------------------|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|------|
| | cag Gln | | | | | | | | | | | | | | | 1545 |
| | tac Tyr 500 | | | _ | | | | | | | | _ | | | | 1593 |
| | gtc Val | | | | | | | | | | | | | | | 1641 |
| | ctg Leu | _ | _ | _ | | _ | | | | | _ | | | | | 1689 |
| _ | atc Ile | _ | | | | | | | | | | | | | | 1737 |
| | tct Ser | | - | | _ | _ | | - | | | | | | | | 1785 |
| | aag Lys 580 | | | | | | | | | | | | | | | 1833 |
| _ | gag Glu | | | | - | - | | | | | _ | | | | | 1881 |
| _ | tac Tyr | _ | _ | | | | | | | - | | - | | | | 1929 |
| Phe | tat Tyr | Phe | Thr 630 | Glu | Leu | Asp | Āla | Lys 635 | Thr | Val | Thr | Ala | Glu 640 | Val | Gln | 1977 |
| | cag Gln | | | | | | | | | | | | | | | 2025 |
| | gga Gly 660 | | | | | | | | | | | | | | | 2073 |
| | ttc Phe | | | | | | | | | | | | | | | 2121 |
| gat | gac | ctg | gtg | aag | atg | ctc | ttc | agc | cca | gaa | gag | atg | gac | ctc | tcc | 2169 |

| Asp Asp Leu Val Lys Met Leu 695 | Phe Ser Pro Glu 700 | Glu Met Asp Leu Ser 705 |
|--|--|---|
| cag gag cag ccc ctg gat gcc Gln Glu Gln Pro Leu Asp Ala 710 | | |
| gag tot oto toa ggo agt gaa Glu Ser Leu Ser Gly Ser Glu 725 | | |
| tgacagcgtc caggtcagac ggatg ctctgagctg gccagcccct cgggg gaggggaccc tgctcacagc cttct gacaccgcac cccctggatc tggct gcctccacag gccgctgcat aacag agaataaatg attcatggtt ttttt | ctgca gagcagtgag acatg gtgctactgc gaggg ctcaggacac cgata cagtacttaa | cctacatctg ccactcagcc 2379 tcttggagtg gacatgacca 2439 aggcccagcc acccccaggg 2499 gtgtctgtgt agacaaccaa 2559 |
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| Ala Ala Ala Ser Gln Ala Glu 20 | | — - |
| Val Thr Pro Asp Leu Leu Phe | | = - |
| Gly Asp Trp Pro Gly Val Val | = = | Arg Ala Leu Arg Ser |
| Arg Ala Ala Leu Arg Ala Leu | Arg Leu Arg Cys | Arg Thr Gln Cys Ala 80 |
| Ala Asp Phe Pro Trp Glu Leu 85 | Asp Pro Asp Trp 90 | Ser Pro Ser Pro Ala 95 |
| Gln Ala Ser Gly Ala Gly Ala 100 | Leu Arg Asp Leu 105 | Ser Phe Phe Gly Gly 110 |
| Leu Leu Arg Arg Ala Ala Cys | Leu Arg Arg Cys 120 | Leu Gly Pro Pro Ala 125 |
| Ala His Ser Leu Ser Glu Glu 130 135 | Met Glu Leu Glu | Phe Arg Lys Arg Ser 140 |
| Pro Tyr Asn Tyr Leu Gln Val | Ala Tyr Phe Lys 155 | |
| Lys Ala Val Ala Ala Ala His | Thr Phe Phe Val | Gly Asn Pro Glu His 175 |
| Met Glu Met Gln Gln Asn Leu 180 | | Thr Met Ser Gly Val |
| Lys Glu Ala Asp Phe Lys Asp | | |
| Phe Arg Leu Gly Val Arg Leu 210 215 | Tyr Ser Glu Glu | |
| Val Pro His Leu Glu Ala Ala 225 230 | | Phe Val Ala Tyr Glu |
| Glu Cys Arg Ala Leu Cys Glu 245 | | |
| Tyr Leu Glu Tyr Asn Ala Asp | | |

| | | | 260 | | | | | 265 | | | | | 270 | | |
|------------|-----|------------|----------|-------|------------|-----|------------|-----|-----|-----|-----|------------|-------|-------|------------|
| Ile | Gln | Val 275 | Leu | Asn | Cys | Lys | Gln 280 | | Cys | Val | Thr | Glu 285 | Leu | Ala | Ser |
| | 290 | Ser | | | Lys | 295 | | | | | 300 | | | | |
| 305 | | | | | Ala 310 | | | | | 315 | | | | | 320 |
| Gly | | | | 325 | Thr | | | | 330 | | | | | 335 | |
| | | | 340 | | Ala | | | 345 | | | | | 350 | | |
| | | 355 | | | Pro | | 360 | | | | | 365 | | | |
| | 370 | | | | Glu | 375 | | | | | 380 | | | | |
| 385 | | | | | Pro 390 | | | | | 395 | | | | | 400 |
| _ | | | | 405 | Lys | | | | 410 | | | | | 415 | |
| | | | 420 | | Gly | | | 425 | | | | | 430 | | |
| | | 435 | | | Glu | | 440 | | | | | 445 | | | |
| _ | 450 | | | | Tyr | 455 | | | | | 460 | | | | |
| 465 | | | | | Gln 470 | | | | | 475 | | | | | 480 |
| | | | | 485 | Leu | | | | 490 | | | | | 495 | |
| _ | | | 500 | | Gly | | | 505 | | | | | 510 | | |
| | | 515 | | | Val | | 520 | | | | | 525 | | | |
| | 530 | | | | Ser | 535 | | | | | 540 | | | | |
| 545 | | | | | 550 | | | | | 555 | | | | | Tyr 560 |
| | | | | 565 | Leu | | | | 570 | | | | | 575 | |
| | | | 580 | | | | | 585 | | | | | 590 | | Ile |
| | | 595 | | | | | 600 | | | | | 605 | | | Thr |
| | 610 | | | | | 615 | | | | | 620 | | | | Gly |
| 625 | | | | | 630 | | | | | 635 | | | | | Glu 640 |
| | | | | 645 | i | | | | 650 | | | | | 655 | |
| | | | 660 |) | | | | 665 | | | | | 670 | | Ile |
| | | 675 | , | | | | 680 | | | | | 685 | | | Val |
| | 690 |) | | | | 695 | , | | | | 700 | | | | Asp |
| Leu 705 | | Gln | ı Glı | ı Glr | 710 | | ı Asp | ATA | GIN | 715 | | PIO | , P10 | . Giu | 720 |

| Ala Gln Glu Ser Leu Ser Gly Ser Glu Ser Lys Pro Lys Asp Glu Leu 725 730 735 | |
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| tgg gac gtg gca gcc cct gac ctg ctt tac gca gag ggg acc gcg gcc Trp Asp Val Ala Ala Pro Asp Leu Leu Tyr Ala Glu Gly Thr Ala Ala 30 35 40 45 | 146 |
| tac tcg cgc agg gac tgg ccc ggg gtg gtc ctg aac atg gag cgg gct Tyr Ser Arg Arg Asp Trp Pro Gly Val Val Leu Asn Met Glu Arg Ala 50 55 60 | 194 |
| ctg cgc tcg cgg gcg gcc ctg cgt gcc ctc cgc ctg cgc tgc cgc aca Leu Arg Ser Arg Ala Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr 65 70 75 | 242 |
| cgc tgt gcc acc gaa ctg ccg tgg gca ccg gac ctg gat ctc ggt ccg Arg Cys Ala Thr Glu Leu Pro Trp Ala Pro Asp Leu Asp Leu Gly Pro 80 85 90 | 290 |
| gac ccc agc ctg agc cag gac ccg ggc gcc gcc ctg cac gac ctg Asp Pro Ser Leu Ser Gln Asp Pro Gly Ala Ala Ala Leu His Asp Leu 95 100 105 | 338 |
| cgc ttc ttc gga gcc gtg ctg cgc cgt gcc gcc tgc cta cgc cgc tgc Arg Phe Phe Gly Ala Val Leu Arg Arg Ala Ala Cys Leu Arg Arg Cys 110 125 | 386 |
| ctc ggg ccg ccc tct gcc cac ttg ctg agt gaa gaa ctg gac ctg gag Leu Gly Pro Pro Ser Ala His Leu Leu Ser Glu Glu Leu Asp Leu Glu 130 135 140 | 434 |
| ttc aac aag cgg agc ccg tac aac tac ctg cag gtc gcc tat ttc aag Phe Asn Lys Arg Ser Pro Tyr Asn Tyr Leu Gln Val Ala Tyr Phe Lys 145 150 155 | 482 |

| ata a Ile A | aac Asn | aag Lys 160 | ctg Leu | gag Glu | aaa Lys | gct Ala | gtg Val 165 | gct Ala | gcg Ala | gca Ala | cac His | acc Thr 170 | ttc Phe | ttt Phe | gtg Val | 530 | |
|-----------------------|------------|-------------------|------------|------------|-------------------|------------|-------------------|------------|------------|-------------------|------------|-------------------|------------|------------|-------------------|------|---|
| ggc a Gly A 1 | | | | | | | | | | | | | | | | 578 | |
| acc a Thr M 190 | atg Met | tct Ser | ggg ggg | gtg Val | aag Lys 195 | gag Glu | gca Ala | gac Asp | ttc Phe | agg Arg 200 | gat Asp | ctc Leu | gag Glu | gcc Ala | aag Lys 205 | 626 | |
| ccc c Pro H | | | | | | | | | | | | | | | | 674 | |
| aag c Lys P | | | | | | | | | | | | | | | | 722 | |
| ttt g Phe V | | | | | | | | | | | | | | | | 770 | |
| tac g Tyr A | | | | | | | | | | | | | | | | 818 | |
| atc a Ile T 270 | | | | | | | | | | | | | | | | 866 | |
| acg g Thr G | | | | | | | | | | | | | | | | 914 | |
| ctc c Leu F | | | | | | | | | | | | | | | | 962 | |
| aac t Asn T | | | | | | | | | | | | | | | | 1010 | 1 |
| ccc a Pro A | | | | | | | | | | | | | | | | 1058 | |
| ctt g Leu G 350 | gga Gly | gaa Glu | gaa Glu | gag Glu | gcc Ala 355 | agc Ser | tcc Ser | atc Ile | agc Ser | ccc Pro 360 | agg Arg | gag Glu | aat Asn | gcc Ala | gag Glu 365 | 1106 | |
| gaa t Glu T | | | | | | | | | | | | | | | | 1154 | : |
| tat g | gac | att | ttt | gga | att | ccc | ttt | gtg | gat | ccc | gat | tca | tgg | act | cca | 1202 | : |

| Tyr | Asp | Ile | Phe 385 | | Ile | Pro | Phe | Val 390 | | Pro | Asp | Ser | Trp 395 | Thr | Pro | |
|------------|------------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|------|
| | | | | | | aga Arg | | | | | | | | | cgg Arg | 1250 |
| gaa Glu | aca Thr 415 | Ala | gta Val | cgc Arg | atc Ile | tcc Ser 420 | cag Gln | gag Glu | att Ile | gly aaa | aac Asn 425 | ctt Leu | atg Met | aag Lys | gaa Glu | 1298 |
| | | | | | | gag Glu | | | | | | | | | | 1346 |
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| acc Thr | atg Met | aac Asn | tcc Ser 465 | aaa Lys | gtc Val | ttg Leu | aat Asn | ggc Gly 470 | tcc Ser | cag Gln | cgg Arg | gtg Val | gtg Val 475 | atg Met | gat Asp | 1442 |
| ggt Gly | gtg Val | atc Ile 480 | tct Ser | gat Asp | gat Asp | gag Glu | tgc Cys 485 | cag Gln | gag Glu | ctg Leu | cag Gln | aga Arg 490 | ctg Leu | acc Thr | aat Asn | 1490 |
| | | | | | | gat Asp 500 | | | | | | | | | | 1538 |
| | | | | | | tat Tyr | | | | | | | | | | 1586 |
| ctc Leu | gl ^à aaa | cag Gln | gaa Glu | gga Gly 530 | aaa Lys | gtt Val | cct Pro | ctg Leu | cag Gln 535 | agt Ser | gcc Ala | cgc Arg | atg Met | tac Tyr 540 | tac Tyr | 1634 |
| | | | | | | cgg Arg | | | | | | | | | | 1682 |
| gac Asp | acg Thr | ccc Pro 560 | ctc Leu | tat Tyr | ttc Phe | tct Ser | tat Tyr 565 | tcc Ser | cac His | ttc Phe | gtg Val | tgc Cys 570 | cgc Arg | act Thr | gca Ala | 1730 |
| | | | | | | gag Glu 580 | | | | | | | | | | 1778 |
| | | | | | | aat Asn | | | | | | | | | | 1826 |
| | | | | | | cgg Arg | | | | | | | | | | 1874 |

620 615 610 ggc gac ttc gat gga gga aac ttt tac ttc aca gaa cta gat gcc aag 1922 Gly Asp Phe Asp Gly Gly Asn Phe Tyr Phe Thr Glu Leu Asp Ala Lys 630 1970 act gtg acg gca gag gtg cag ccc cag tgt gga agg gct gtg gga ttc Thr Val Thr Ala Glu Val Gln Pro Gln Cys Gly Arg Ala Val Gly Phe 645 640 2018 tet tet gge act gag aac eea cat gga gtg aag get gte ace agg ggg Ser Ser Gly Thr Glu Asn Pro His Gly Val Lys Ala Val Thr Arg Gly 665 660 655 cag cgc tgc gcc atc gcc ctg tgg ttc acg ctg gat cct cgg cac agt 2066 Gln Arg Cys Ala Ile Ala Leu Trp Phe Thr Leu Asp Pro Arg His Ser 675 670 gag aga gac agg gtg cag gca gat gac ctg gtg aag atg ctg ttc agc 2114 Glu Arg Asp Arg Val Gln Ala Asp Asp Leu Val Lys Met Leu Phe Ser 695 690 cca gaa gag gtg gac ctc ccc cag gaa cag ccc ctg cct gac cag cag 2162 Pro Glu Glu Val Asp Leu Pro Gln Glu Gln Pro Leu Pro Asp Gln Gln 715 705 ggt tcg cca gag cct gga gaa gag ttt ctg cat ggt gct act gtt ctt 2210 Gly Ser Pro Glu Pro Gly Glu Glu Phe Leu His Gly Ala Thr Val Leu 725 720 2252 gga gtg ggc ata gca gga cac act ctt ctc tgg gct tgg ctg Gly Val Gly Ile Ala Gly His Thr Leu Leu Trp Ala Trp Leu taggeteaga atgeaggeee agaaceaeee tggggeetat gtaggeaget geegteagea 2312 gcgtgatata tttaagtgtc tgtaaagaca accaaagaat aaatgatttg tgtttttaaa 2372 2416 aagnaaaaaa aaaaaaaaat taaaaatttg cgcggccgca agaa <210> 6 <211> 747 <212> PRT <213> Mus musculus <400> 6 Met Ala Val Thr Lys Gly Gly Cys Trp His Asp Ala Ser Gly Arg Arg 10 Arg Arg Arg Leu Thr Gly Cys Gly Glu Ser Glu Pro Gly Trp Asp Val 25 Ala Ala Pro Asp Leu Leu Tyr Ala Glu Gly Thr Ala Ala Tyr Ser Arg 40 Arg Asp Trp Pro Gly Val Val Leu Asn Met Glu Arg Ala Leu Arg Ser 55 Arg Ala Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr Arg Cys Ala 75 70 Thr Glu Leu Pro Trp Ala Pro Asp Leu Asp Leu Gly Pro Asp Pro Ser 90 Leu Ser Gln Asp Pro Gly Ala Ala Ala Leu His Asp Leu Arg Phe Phe

| | | | 100 | | | | | 105 | | | | | 110 | | |
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| Gly | Ala | Val 115 | Leu | | Arg | Ala | Ala 120 | | | Arg | Arg | Cys 125 | Leu | | Pro |
| Pro | Ser 130 | Ala | His | Leu | Leu | Ser 135 | Glu | Glu | Leu | Asp | Leu 140 | Glu | Phe | Asn | Lys |
| Arg 145 | Ser | Pro | Tyr | Asn | Tyr 150 | Leu | Gln | Val | Ala | Tyr 155 | Phe | Lys | Ile | Asn | Lys 160 |
| | | | Ala | 165 | | | | | 170 | | | | _ | 175 | |
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| | | | Сув | 245 | | | | | 250 | | | | | 255 | |
| | | | Leu 260 | | | | | 265 | | | | | 270 | | - |
| | | 275 | Gln | | | | 280 | | | | | 285 | | | |
| | 290 | | Pro | | | 295 | | | | | 300 | | | | |
| 305 | | | Tyr | | 310 | | | | | 315 | | | | _ | 320 |
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| | 450 | | Gly | | | 455 | | | | | 460 | | | | |
| 465 | | | Leu | | 470 | | | | | 475 | | | | | 480 |
| | | | Glu | 485 | | | | | 490 | | | | | 495 | |
| | | | Asp 500 | | | | | 505 | | | | | 510 | | |
| | | 515 | Tyr | | | | 520 | | | | | 525 | | | |
| | 530 | | Val | | | 535 | | | | | 540 | _ | | | |
| Glu 545 | Lys | Val | Arg | Arg | Val 550 | Met | Glu | Ser | | Phe 555 | Arg | Leu | Asp | Thr | Pro 560 |

| Let | ı Tyr | Phe | Ser | Tyr 565 | | His | Phe | · Val | Cys 570 | Arg | Thr | Ala | Ile | Glu 575 | | |
|----------------------------------|--|--------------------------------|---------------------|-------------------|------------------|-----------------------|------------|------------|-----------------------|----------------------|-----------------------|----------------|-----------------------|----------------|------------------|-----|
| Sei | Gln | Ala | Glu 580 | | Lys | Asp | Ser | Ser 585 | | Pro | Val | His | Val 590 | | | |
| Cys | s Ile | Leu 595 | | Ala | Glu | Ala | Phe 600 | Met | | Ile | Lys | Glu 605 | | Pro | Ala | |
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| Asp 625 | Gly | Gly | Asn | Phe | Tyr 630 | | Thr | Glu | Leu | Asp 635 | | Lys | Thr | Val | Thr 640 | |
| Ala | Glu | Val | Gln | Pro 645 | | Cys | Gly | Arg | Ala 650 | | Gly | Phe | Ser | Ser 655 | Gly | |
| Thr | Glu | Asn | Pro 660 | | Gly | Val | Lys | Ala 665 | | Thr | Arg | Gly | Gln 670 | Arg | Cys | |
| Ala | Ile | Ala 675 | | Trp | Phe | Thr | Leu 680 | | Pro | Arg | His | Ser 685 | | Arg | Asp | |
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| Val 705 | Asp | | Pro | Gln | Glu 710 | | Pro | Leu | Pro | Asp 715 | | Gln | Gly | Ser | | |
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| <21 <22 <22 <22 <22 <22 <22 <400 | 1> CI 2> (3 1> mi 2> 22 3> n | NA LS MU OS L2) LSC_f 282 = A, | .(16 eatu T,C | 37) re or 0 | | | | | | | | | | | | |
| | gcaag | | Met 1 | Ala | . Val | Thr | Lys 5 | Gly | Gly | Cys | Trp | His 10 | Asp | Ala | Ser | 50 |
| ggt Gly | cgc Arg 15 | cgc Arg | cgc Arg | cgc Arg | cgc Arg | ctt Leu 20 | acg Thr | ggt Gly | tgc Cys | ggc Gly | gag Glu 25 | tct · Ser · | gag (Glu 1 | ccg Pro | gga Gly | 98 |
| tgg Trp 30 | gac Asp | gtg Val | gca Ala | gcc Ala | cct Pro 35 | gac Asp | ctg Leu | ctt Leu | tac : Tyr . | gca (Ala (40 | gag (Glu (| gly ' | acc o | gcg (Ala | gcc Ala 45 | 146 |
| tac Tyr | tcg Ser | cgc Arg | agg Arg | gac Asp 50 | tgg Trp | ccc (Pro (| Gly 999 | gtg Val | gtc Val : 55 | ctg a Leu A | aac a Asn 1 | atg (Met (| gag o Glu <i>l</i> | egg (Arg 1 | gct Ala | 194 |
| ctg Leu | cgc Arg | tcg Ser | cgg (Arg) | gcg (Ala | gcc Ala : | ctg (Leu <i>l</i> | cgt Arg | gcc Ala | ctc (Leu <i>i</i> | ege (Arg 1 | ctg (Leu <i>l</i> | ege (Arg (| tgc d Cys <i>I</i> | ege a Arg : | aca Thr | 242 |

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| cto Leu | cct Pro | tca Ser | cac His | Tyr | aat Asn | tac Tyr | cta Leu | cag Gln 310 | Phe | gcc Ala | tac Tyr | tac Tyr | aac Asn 315 | Ile | : Gly | 962 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| aac Asn | tat Tyr | aca Thr 320 | Gln | gct Ala | att Ile | gaa Glu | tgt Cys 325 | gcc Ala | aag Lys | acc Thr | tac Tyr | ctc Leu 330 | Leu | ttc Phe | ttt Phe | 1010 |
| ccc Pro | aat Asn 335 | Asp | gag Glu | gtg Val | atg Met | cac His 340 | cag Gln | aat Asn | ctg Leu | gct Ala | tat Tyr 345 | Tyr | aca Thr | gcc Ala | atg Met | 1058 |
| ctt Leu 350 | gga Gly | gaa Glu | gaa Glu | gag Glu | gcc Ala 355 | agc Ser | tcc Ser | atc Ile | agc Ser | ccc Pro 360 | agg Arg | gag Glu | aat Asn | gcc Ala | gag Glu 365 | 1106 |
| gaa Glu | tac Tyr | cga Arg | cgt Arg | cca Pro 370 | aac Asn | ctg Leu | ttg Leu | gag Glu | aaa Lys 375 | gaa Glu | ctg Leu | ctt Leu | ttc Phe | ttc Phe 380 | gct Ala | 1154 |
| tat Tyr | gac Asp | att Ile | ttt Phe 385 | gga Gly | att Ile | ccc Pro | ttt Phe | gtg Val 390 | gat Asp | ccc Pro | gat Asp | tca Ser | tgg Trp 395 | act Thr | cca Pro | 1202 |
| gaa Glu | gaa Glu | gtg Val 400 | att Ile | ccc Pro | aag Lys | aga Arg | ttg Leu 405 | caa Gln | gag Glu | aaa Lys | cag Gln | aag Lys 410 | tct Ser | gaa Glu | cgg Arg | 1250 |
| gaa Glu | aca Thr 415 | gcc Ala | gta Val | cgc Arg | atc Ile | tcc Ser 420 | cag Gln | gag Glu | att Ile | gly aaa | aac Asn 425 | ctt Leu | atg Met | aag Lys | gaa Glu | 1298 |
| atc Ile 430 | gag Glu | acc Thr | ctt Leu | gtg Val | gaa Glu 435 | gag Glu | aag Lys | acc Thr | aag Lys | gag Glu 440 | tct Ser | ctg Leu | gat Asp | gtg Val | agc Ser 445 | 1346 |
| aga Arg | ctg Leu | acc Thr | cgg Arg | gaa Glu 450 | ggt Gly | ggt Gly | ccc Pro | ctg Leu | ctg Leu 455 | tat Tyr | gaa Glu | ggc Gly | atc Ile | agt Ser 460 | ctc Leu | 1394 |
| acc Thr | atg Met | aac Asn | tcc Ser 465 | aaa Lys | gtc Val | ttg Leu | aat Asn | ggc Gly 470 | tcc Ser | cag Gln | cgg Arg | gtg Val | gtg Val 475 | atg Met | gat Asp | 1442 |
| ggt Gly | gtg Val | atc Ile 480 | tct Ser | gat Asp | gat Asp | Glu | tgc Cys 485 | cag Gln | gag Glu | ctg Leu | cag Gln | aga Arg 490 | ctg Leu | acc Thr | aat Asn | 1490 |
| gcg Ala | gca Ala 495 | gca Ala | act Thr | tcg Ser | Gly | gat Asp 500 | ggc Gly | tac Tyr | cga Arg | ggt Gly | cag Gln 505 | acc Thr | tcc Ser | cca Pro | cac His | 1538 |
| acc Thr 510 | cca Pro | aat Asn | gaa Glu | Lys | ttc Phe 515 | tat Tyr | ggt Gly | gtt Val | Thr | gtc Val 520 | ctc Leu | aaa Lys | gct Ala | ctc Leu | aag Lys 525 | 1586 |

| ct Le | c gg u Gl | g ca y Gl: | g ga n Gl | a gg u Gl 53 | у Lу | a gt s Va | t cc l Pr | t ct | g ca u Gl 53 | n Se | t go r Al | c cg a Ar | c ac g Th | c gc r Ala 54 | a ctg a Leu 0 | 1634 |
|--|--|--|--|--|--|---|---|--|--|---|------------------------------|---|---|--|--|--|
| ca: Gl: | a ta n | gaag | agtc | aca | ggct | gag a | agga | agga | ca g | tagc | cacc | c cg | tcca | cgtg | | 1687 |
| tto gto cgo cao cao act aat aat | cegge cacae ggga ctgce ggte cgtte cgcae ctaae | gaat gaac ttet geca gatg etge ettg ggcc gtgt | taga ctto ctga ctga ctga caga ctgt | gege atge etgge eeete tggte accae tggge aacca | cat (caa (caa (caa (caa (caa (caa (caa (| cetti gaete gaga gttea gggtt ageae etgge aacea | cacer gtgadaced acger ctgtt ccgcd ggaca ggcct | to as constant of the constant | atgg atgga atgga atcc geca geca get atct aga ata ata ata ata ata ata ata ata at | cgac ggtgagtga tcgga agaag tggag tctct | t togage agg agg agg tgg tgg | gatgg cccca gctgf agtga gtgga gagtt gcttg | gagg agtg tcac agag acct tct ggct | aaad tgga cagg agad cccc gcat gtag | atacacg cttttac aagggct ggggcag cagggtg ccaggaa cggtgct ggctcag gtgatat ynaaaaa | 1747 1807 1867 1927 1987 2047 2107 2167 2227 2287 2322 |
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| _ | _ | | Thr | Lys 5 | Gly | Gly | Cys | Trp | His | a Asp | Ala | Ser | Gly | | Arg | |
| | Arg | Arg | Leu 20 | _ | Gly | Cys | Gly | Glu 25 | | Glu | Pro | Gly | Trp | 15 Asp | Val | |
| Ala | Ala | Pro | Asp | Leu | Leu | Tyr | Ala 40 | | Gly | Thr | Ala | Ala | . Tyr | Ser | Arg | |
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| 65 | | | | | 70 | | | Leu | | 75 | | | | | 80 | |
| | | | | 85 | | | | Leu | 90 | | | | | 95 | Ser | |
| | | | 100 | | | | | Ala 105 | | | | | 110 | | | |
| | | 115 | | | | | 120 | Cys | | | | 125 | Leu | | | |
| | 130 | | | | | 135 | | Glu | | | 140 | | | | | |
| 145 | | | | | 150 | | | Val | | 155 | | | | | 160 | |
| Leu | Glu | Lys | Ala | Val 165 | Ala | Ala | Ala | His | Thr 170 | Phe | Phe | Val | Gly | Asn 175 | Pro | |
| | | | 180 | | | | | Leu 185 | Asp | | | | 190 | Met | | |
| | | 195 | | | | | 200 | Asp | | | | 205 | Pro | | | |
| | 210 | | | | | 215 | | Leu | | | 220 | Glu | | | | |
| Glu | Ala | Val | Pro | His | Leu | Glu | Ala | Ala | Leu | Gln | Glu | Tyr | Phe | Val | Ala | |
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 His Tyr Val Gln Val Leu Asn Cys Lys Gln Asn Cys Val Thr Glu Leu
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 Ala Ser His Pro Ser Arg Glu Lys Pro Phe Glu Asp Phe Leu Pro Ser
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 His Tyr Asn Tyr Leu Gln Phe Ala Tyr Tyr Asn Ile Gly Asn Tyr Thr
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Glu Glu Ala Ser Ser Ile Ser Pro Arg Glu Asn Ala Glu Glu Tyr Arg
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Arg Pro Asn Leu Leu Glu Lys Glu Leu Leu Phe Phe Ala Tyr Asp Ile
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Phe Gly Ile Pro Phe Val Asp Pro Asp Ser Trp Thr Pro Glu Glu Val
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